Access DB# 76122

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's full Name: Everett White Examiner #: 67057 Date: 9/29/2002
Art Unit: 1623 Phone Number 308-4621 Serial Number: PCT/US02/25028 / 09/915,333
Mail Box: CM1-8B19 and Bldg/Room Location: CM1-7B13 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be search Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: See copy of Front Cover

Inventors (please provide full names): See copy of Front Cover

Earliest priority Filing Date: See copy of Front Cover

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search the method of exfoliating the skin of Claims 1-6, the method for increasing levels of glycosaminoglycans in skin of Claims 7-12, the method of treating a skin condition associated with a reduced level of glycosaminoglycans in the skin of Claims 13-19. A copy of the claims is provided.

The copy of the front cover discloses the title of the invention and the earliest priority filing date.

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: P. Schwab	NA Sequence (#)	STN 7424
Searcher Phone #: 305-4232	AA Sequence (#)	Dialog
Searcher Location: CM1 6B13	Structure (#)	Questel/Orbit
Date Searcher Picked Up:	Bibliographic V	Dr. Link
Date Completed: 9/25	Litigation	Lexis/Nexis
Searcher Prep & Review Time: 3.7	Fulltext	Sequence Systems
Clerical prep time:	Patent Family	WWW/Internet
Online Time: 3.7	Other	Other (specify)

PTO-1590 (1-2000)

White PCT/US02/25028

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=> d his 1

     (FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     15:21:25 ON 25 SEP 2002)
L22          20 DUP REM L21 (1 DUPLICATE REMOVED)

=> d que l22
L1         3257 SEA EXFOLIAT? (3A)(SKIN OR DERM? OR EPIDERM?)
L2          141 SEA PHOSPHOSUGAR#
L3         7508 SEA PHOSPHATE(3A) SUGAR#
L4       121809 SEA PHOSPHATE(3A)(GLUCOS? OR MANNOS? OR GALACTOS? OR FRUCTOS?)

L5        91760 SEA (TREAT? OR THERAP?) (5A) (SKIN OR DERM? OR EPIDERM?)
L6         3700 SEA (LEVEL# OR AMOUNT# OR CONCENTRATION#)(5A) GLYCOSAMINOGLYCAN
                #
L13         174 SEA PHOSPHO(A) SUGAR#
L14       39489 SEA MUCOPOLYSACCHARID?
L15           3 SEA L1 AND ((L2 OR L3 OR L4) OR L13)
L16         107 SEA L5 AND ((L2 OR L3 OR L4) OR L13)
L17          16 SEA L16 AND ((L7 OR L8 OR L9 OR L10 OR L11 OR L12))
L18         940 SEA (LEVEL# OR AMOUNT# OR CONCENTRATION#)(5A) L14
L19         182 SEA (L18 OR L6)(5A)(SKIN# OR DERM? OR EPIDERM?)
L20           2 SEA L19 AND ((L2 OR L3 OR L4) OR L13)
L21          21 SEA L15 OR L17 OR L20
L22          20 DUP REM L21 (1 DUPLICATE REMOVED)


=> d ibib abs l22 1-20

L22  ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2002:594822  HCAPLUS
DOCUMENT NUMBER:         137:154857
TITLE:                   Preparation of nicotinamide biaryl derivatives as
                         inhibitors of PDE4 isozymes
INVENTOR(S):             Chambers, Robert James; Magee, Thomas Victor; Marfat,
                         Anthony
PATENT ASSIGNEE(S):      Pfizer Productors Inc., USA
SOURCE:                  PCT Int. Appl., 224 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002060875      A1   20020808       WO 2001-IB2341   20011206
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  US 2001-265492P  P  20010131
OTHER SOURCE(S):         MARPAT 137:154857
GI
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Search completed by David Schreiber 308-4292

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; g = 0-1; j = 0-1; provided that when j = 0, n must be 2; k = 0-1; m = 0-2; n = 1-2; W1 = 0, SOt (t = 0-2), NR3; W2 = OCR9R10, or absent; Y = CR1, NOk (k = 0-1); R9, R10 = H, F, CF3, etc.; or R9 and R10 are taken together, but only in the case where m = 1, to form a spiro moiety; R7, R8 have the same meaning as R9, R10 except that one of them must be H; R1, R2 = H, F, Cl, etc.; R3 = H, alkyl, Ph, etc.; R4-R6 = H, F, Cl, etc.; Q1 = Ph, benzodioxyl, etc.; Q2 = biaryl moiety], useful as inhibitors of PDE4 in the treatment of diseases regulated by the activation and degranulation of eosinophils, esp. asthma, chronic bronchitis, and chronic obstructive pulmonary disease, were prepd. E.g., a multi-step synthesis of the amide II, starting from Me 3-bromobenzoate and 4-formylbenzeneboronic acid, was given. Compds. I showed anti-inflammatory activity at 0.0001 .mu.M to 20.0 .mu.M in whole blood assay for LTE4.

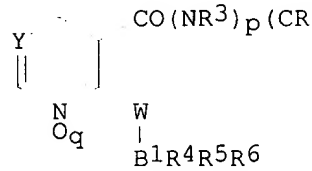
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:591707 HCAPLUS
DOCUMENT NUMBER: 137:140509
TITLE: Preparation of nicotinamides and mimetics as inhibitors of phosphodiesterase IV isozymes
INVENTOR(S): Chambers, Robert J.; Magee, Thomas V.; Marfat, Anthony
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 180 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1229034	A1	20020807	EP 2002-250202	20020111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002111495	A1	20020815	US 2002-62811	20020131

PRIORITY APPLN. INFO.: US 2001-265240P P 20010131
US 1997-43403P P 19970404
US 1998-105120P P 19981021

OTHER SOURCE(S): MARPAT 137:140509
GI



I

AB Title compds. [I; p, q = 0, 1; m = 0-2; n = 1, 2; A = CO2R7, CONR9CO2R7, CONR7R9, OP(O)(OH)2, SO3H, acylsulfonamido, etc.; W = O, S, SO, SO2, NR3; Y = N, NO, CR11; R1, R2 = H, F, Cl, cyano, NO2, alkyl, alkynyl, fluoroalkyl, etc.; R3 = H, alkyl, Ph, PhCH2, etc.; R4-R6 = H, F, Cl, alkynyl, cyano, NO2, etc.; R7 = H, (substituted) alkyl, alkenyl, alkynyl; R9 = H, alkyl, cycloalkyl, Ph, PhCH2, pyridyl, etc.; R11 = H, F, Cl, cyano, NO2, alkyl, alkynyl, fluoroalkyl, fluoroalkoxy, etc.; Ra, Rb = H, F, CF3, alkyl, (substituted) cycloalkyl, Ph, PhCH2; B1, B2 = 3-7 membered (hetero)cyclyl, 7-12 membered poly(hetero)cyclyl; pairs of variables may form rings; with provisos], were prepd. (no data). Thus, Me 2-[4-[[[2-(benzo[1,3]dioxol-5-yloxy)pyridine-3-carbonyl]amino]methyl]phenyl]-2-methylpropionate was suspended in Me3COH. Aq. NaOH was added to the suspension, and the reaction mixt. was refluxed 1 h to give 2-[4-[[[2-(benzo[1,3]dioxol-5-yloxy)pyridine-3-carbonyl]amino]methyl]phenyl]-2-methylpropionic acid.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:353023 HCAPLUS
DOCUMENT NUMBER: 135:162661
TITLE: Suppression of 12-O-tetradecanoylphorbol-13-acetate-induced epidermal hyperplasia and inflammation by the dehydroepiandrosterone analog 16.alpha.-fluoro-5-androsten-17-one and its reversal by NADPH liposomes
AUTHOR(S): Schwartz, A. G.; Pashko, L. L.
CORPORATE SOURCE: Department of Microbiology, Temple University School of Medicine, Philadelphia, PA, 19140, USA
SOURCE: Cancer Letters (Shannon, Ireland) (2001), 168(1), 7-14
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dehydroepiandrosterone and related steroids produce cancer-preventive and other potentially important therapeutic effects in lab. animals. These steroids are potent uncompetitive inhibitors of mammalian **glucose -6-phosphate** dehydrogenase, the first enzyme in the pentose phosphate pathway. Inhibition of this pathway could have profound effects on the supply of 5-carbon sugars required for nucleic acid synthesis as well as on the availability of NADP (NADPH) and the cellular redox state. NADPH is a source of reducing equiv. for the prodn. of oxygen free radicals, which act as intermediate messengers stimulating mitogenesis and up-regulating the inflammatory response. Using a mixt. of NADPH and cationic liposomes to facilitate uptake of the normally impenetrable dinucleotide, the authors found that intradermal injections of NADPH-liposomes reversed the anti-inflammatory and anti-hyperplastic effects of the dehydroepiandrosterone analog, 16.alpha.-fluoro-5-androsten-17-one, in mouse **skin treated** with 12-O-tetradecanoylphorbol-13-acetate, whereas similar treatment had no apparent effect on the anti-hyperplastic and anti-inflammatory effect of corticosterone.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 20 MEDLINE
ACCESSION NUMBER: 2001149155 MEDLINE
DOCUMENT NUMBER: 21083085 PubMed ID: 11214480
TITLE: [What do we know today about diaminodiphenylsulfone?]. Sta danas znamo o diaminodifenilsulfonu?.

Search completed by David Schreiber 308-4292

AUTHOR: Golusin Z; Poljacki M; Preveden R; Stojanovic S; Rajic N
CORPORATE SOURCE: Klinika za kozno-venericne bolesti, Medicinski fakultet, Klinicki centar, Novi Sad.
SOURCE: MEDICINSKI PREGLED, (2000 Jul-Aug) 53 (7-8) 369-72. Ref: 28
Journal code: 2985249R. ISSN: 0025-8105.
PUB. COUNTRY: Yugoslavia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Serbo-Croatian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010315

AB INTRODUCTION: Diaminodiphenylsulfone or dapsone is a chemical analogue of sulfapyridine, synthesized in 1908. Dapsone is a bacteriostatic agent that proved to be efficient in treating leprosy and malaria, but today it is used in **treating dermatologic** noninfectious inflammatory diseases. PHARMACOLOGY: Dapsone is orally used in a dose of 50-400 mg per day in **treatment** of **dermatologic** diseases, and also in a dose of 50-100 mg per day in leprosy treatment. Dapsone is mainly eliminated from the body by urine and smaller part by faeces. Pharmacological interaction was reported when it is used with rifampicin and probenecid. MECHANISM OF ACTION: The bacteriostatic effect of dapsone is well known. It involves inhibition of folic acid synthesis in susceptible organisms. The anti-inflammatory effect of dapsone, which proves to be efficient in treating noninfectious inflammatory diseases, has not been explained completely yet. There are some pieces of evidence that anti-inflammatory action is not connected with its antibacteriological action. CLINICAL USE: Based on previous studies about therapy efficiency of dapsone in treating some diseases, there are two groups of diseases: the group responding well to dapsone (leprosy, malaria, DH, linear IgA-dermatosis, erythema elevatum diutinum, bullous systemic lupus erythematosus) and a group responding with average good response to dapsone (pyoderma gangrenosum, bullous and cicatricial pemphigoid, acne conglobata, discoid cutaneous lupus erythematosus, subcorneal pustulosis dermatosis, granuloma faciale, rheumatoid arthritis, polychondritis, leucocytoclastic vasculitis). ADVERSE EFFECTS: Adverse effects depend on the dose and they rarely occur at doses less than 100 mg per day. They are mainly shown on skin, nervous system, digestive system, hepatobiliary system, and kidney and hematologic system. The most important adverse effects are hemolytic anaemia and methemoglobinemia. Hemolysis usually occurs at doses of 200 mg and more per day. In patients with **glucose**-6-**phosphate** dehydrogenase deficiency, hemolysis may be provoked by a dose less than 50 mg per day. For prevention, before using dapsone in therapy, clinical examination with history, blood parameters, liver and renal parameters and determination of **glucose**-6-**phosphate** dehydrogenase level are recommended. CONCLUSION: The use of dapsone is absolutely indicated in DH treatment and erythema elevatum diutinum. Because of anti-inflammatory effects, dapsone can also be used in **treating** other inflammatory noninfectious **dermatoses** when one should take care about "therapy efficiency/adverse effect" balance using the correct dose, monitoring relevant clinical and laboratory parameters and educating patients.

L22 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:47077 HCAPLUS

Search completed by David Schreiber 308-4292

DOCUMENT NUMBER: 132:303452
TITLE: Enzymatic corrections for cells derived from Fabry disease patients by a recombinant adenovirus vector
AUTHOR(S): Ohsugi, Keiko; Kobayashi, Keiko; Itoh, Kohji; Sakuraba, Hitoshi; Sakuragawa, Norio
CORPORATE SOURCE: Department of Inherited Metabolic Disease, National Center of Neurology and Psychiatry, National Institute of Neuroscience, Tokyo, 187-8502, Japan
SOURCE: Journal of Human Genetics (2000), 45(1), 1-5
CODEN: JHGEFR; ISSN: 1434-5161
PUBLISHER: Springer-Verlag Tokyo
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fabry disease is an X-linked inherited metabolic disorder caused by a deficiency of .alpha.-galactosidase (.alpha.-gal), resulting in the accumulation of ceramide trihexoside (CTH) in body fluids and in many organs and tissues. The authors constructed a recombinant adenovirus with a human .alpha.-gal cDNA (AxCAG .alpha.-gal), and transfected this vector to skin fibroblasts from Fabry patients. Transfected cells expressed high amts. of .alpha.-gal in their cytoplasm, and a high level of .alpha.-gal activity was detected in the medium. The accumulated CTH in the fibroblasts disappeared 3 days after infection. The secreted .alpha.-gal also eliminated the accumulated CTH from uninfected patient's cells. The enzyme may be taken up through **mannose**-6-**phosphate** receptors, as the addn. of **mannose**-6-**phosphate** to the medium completely inhibited the uptake of the enzyme. The infected cells continued to express .alpha.-gal for more than 10 days. These results suggest that AxCAG .alpha.-gal could be used as enzyme replacement gene therapy for Fabry disease.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 20 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999222137 EMBASE
TITLE: Development of dapsone toxicity in patients with inflammatory dermatoses: Activity of acetylation and hydroxylation of dapsone as risk factors.
AUTHOR: Bluhm R.E.; Adedoyin A.; McCarver D.G.; Branch R.A.
CORPORATE SOURCE: Dr. R.A. Branch, Center for Clinical Pharmacology, 620-636 Scaife Hall, Univ. of Pittsburgh Sch. of Medicine, Pittsburgh, PA 15261, United States
SOURCE: Clinical Pharmacology and Therapeutics, (1999) 65/6 (598-605).
Refs: 33
ISSN: 0009-9236 CODEN: CLPTAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: Alternative independent routes of dapsone metabolism include N-hydroxylation to the hydroxylamine, a potentially toxic metabolite, by cytochrome P450 enzymes and acetylation to a nontoxic metabolite by N-acetyltransferase. Potentially, therefore, the relative extents of these two routes in an individual could determine the occurrence of adverse reaction with dapsone therapy. Methods: Phenotypic activity of these two

routes of metabolism was assessed in 18 patients receiving long-term dapsone **therapy** for inflammatory **dermatoses** and was related to the development of dapsone toxicity. N-Hydroxylation was assessed by the dapsone recovery ratio, a ratio of dapsone hydroxylamine to the sum of hydroxylamine and dapsone in 8-hour urine, whereas N-acetylation was assessed by the acetylation ratio, a ratio of monoacetyldapsone to dapsone in 8-hour plasma sample after an oral dose of dapsone. Results: There was wide intersubject variation in both the acetylation ratio and the dapsone recovery ratio, but both phenotypic measures remained stable within individuals. The dapsone recovery ratio showed a tendency toward being lower in fast than in slow acetylators, but this was not statistically significant. There was an inverse relationship between acetylation and hydroxylation ($r = -0.69$; $P < .005$) at steady state that was not apparent after the first dose. Neurotoxicity developed in two subjects and hemolytic anemia developed in two subjects. Plasma levels of dapsone in these four subjects were similar to those in subjects who showed no toxicity. All four were slow acetylators and three were rapid hydroxylators, consistent with the toxic nature of dapsone hydroxylamine. Conclusions: These observations are consistent with what is known about the toxicity profile of dapsone metabolites and suggest that assessing N- acetylation and N-hydroxylation capacities can help to identify subjects at increased risk of a toxic response. This approach of assessing the phenotypic measures of drug-metabolizing activity to predict adverse reaction may also apply to other drugs with metabolic-based adverse effects.

L22 ANSWER 7 OF 20 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97147777 EMBASE
DOCUMENT NUMBER: 1997147777
TITLE: Colchicine as a novel **therapeutic** agent in chronic bullous **dermatosis** of childhood.
AUTHOR: Banodkar D.D.; Al-Suwaid A.R.
CORPORATE SOURCE: Dr. D.D. Banodkar, Baushar Clinic, Al Harthy Complex, PO Box 77, Muscal, Oman
SOURCE: International Journal of Dermatology, (1997) 36/3 (213-216).
Refs: 19
ISSN: 0011-9059 CODEN: IJDEBB
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background. The **treatment** of chronic bullous **dermatosis** of childhood (CBDC) so far has been limited to the use of corticosteroids and the sulfa group of drugs, e.g. daspsone and sulfapyridine. Furthermore, the therapy of CBDC cases with associated G6 PD deficiency is restricted only to systemic steroids. Histopathologically CBDC is characterized by the presence of predominantly neutrophilic infiltration and because it has been proven to exert strong anti-inflammatory effects through the inhibition of neutrophils, colchicine was mandated for its use in CBDC. Methods. To avoid the detrimental side-effects of the long-term use of steroids in children, an alternative anti-inflammatory drug like colchicine was considered. Patients with G6 PD deficiency and those who were not satisfactorily controlled with steroid therapy, and who in addition developed unacceptable side-effects like cushingoid faces and

hypertrichiosis, were treated with the drug. Results. Eight patients were given colchicine, five (62.5%) of which showed complete remission within 4-6 weeks of starting the therapy. The remaining three (37.5%) also responded but required adjuvant small doses of steroids to maintain the remissions. The drug was very well tolerated and no side-effects were observed. Conclusions. Colchicine is, therefore, found to be an effective treatment in CBDC and has enhanced our armamentarium of therapeutics for this condition, especially in children with G6 PD deficiency.

L22 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:454650 HCAPLUS
DOCUMENT NUMBER: 125:139756
TITLE: Arylsulfatase B activities and glycosaminoglycan levels in retrovirally transduced mucopolysaccharidosis type VI cells: prospects for gene therapy
AUTHOR(S): Fillat, Cristina; Simonaro, Calogera M.; Yeyati, Patricia L.; Abkowitz, Janis L.; Haskins, Mark E.; Schuchman, Edward H.
CORPORATE SOURCE: Dep. Human Genetics, Mount Sinai Sch. Med., New York, NY, 10029, USA
SOURCE: Journal of Clinical Investigation (1996), 98(2), 497-502
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mucopolysaccharidosis type VI (MPS VI) is the lysosomal storage disorder caused by the deficient activity of arylsulfatase B (ASB; N-acetylgalactosamine-4-sulfatase) and the subsequent accumulation of the glycosaminoglycan (GAG), dermatan sulfate. In this study, a retroviral vector contg. the full-length human ASB cDNA was constructed and used to transduce skin fibroblasts, chondrocytes, and bone marrow cells from human patients, cats, or rats with MPS VI. The ASB vector expressed high levels of enzymic activity in each of the cell types tested and, in the case of cat and rat cells, enzymic expression led to complete normalization of 35SO4 incorporation. In contrast, overexpression of ASB in human MPS VI skin fibroblasts did not lead to metabolic correction. High-level ASB expression was detected for up to eight weeks in transduced MPS VI cat and rat bone marrow cultures, and PCR anal. demonstrated retroviral-mediated gene transfer to .apprx.30-50% of the CFU GM-derived colonies. Notably, overexpression of ASB in bone marrow cells led to release of the enzyme into the media and uptake by MPS VI cat and rat skin fibroblasts and/or chondrocytes via the **mannose**-6-**phosphate** receptor system, leading to metabolic correction. Thus, these studies provide important rationale for the development of gene therapy for this disorder and lay the frame-work for future in vivo studies in the animal model systems.

L22 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:452310 HCAPLUS
DOCUMENT NUMBER: 122:222867
TITLE: Antioxidants and metabolic regulators for **treatment** of atopic **dermatitis**, pruritis, pruritic psoriasis, photodermatosis, ichthyosis, and hyperreactive **conditions** of sensitive **skin**
INVENTOR(S): Staeb, Franz; Sauermann, Gerhard; Keyhani, Reza
PATENT ASSIGNEE(S): Beiersdorf A.-G., Germany

Search completed by David Schreiber 308-4292

SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4328871	A1	19950302	DE 1993-4328871	19930827
WO 9505852	A1	19950302	WO 1994-EP2831	19940826
W: CN, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 721347	A1	19960717	EP 1994-925480	19940826
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 09501925	T2	19970225	JP 1994-507355	19940826

PRIORITY APPLN. INFO.: DE 1993-4328871 19930827
WO 1994-EP2831 19940826

AB Antioxidants and agents which maintain skin metab. at a normal level and/or regulate the endogenous enzymic antioxidant system are useful for prophylaxis and **treatment** of the title **skin conditions**. Pharmaceuticals and topical prepns. contg. combinations of these agents are provided. Thus, a combination of active agents contained carnosine 3.0, histidine 0.8, urocanic acid 1.0, .beta.-carotene 0.5, palmitoylcystine 0.2, Mg ascorbyl palmitate 2.0, vitamin E acetate 3.5, oleylglutathione 0.2, glucosylcystamine 0.04, oleic acid 0.3, heptadecenoic acid 0.02, butylated hydroxyanisole 0.5, FADH2 0.02, **glucose** 6-**phosphate** 0.06, NADPH 0.05, and ubiquinol 0.5 wt.. parts. A lotion contained this combination 25.00, Cremophor A25 1.000, Cremophor A6 1.000, glycerin mono/distearate 2.000, cetyl alc. 1.000, iso-Pr myristate 1.450, glycerin 1.000, PVP 0.500, and water to 100.000 wt.%.

L22 ANSWER 10 OF 20 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94128868 EMBASE
DOCUMENT NUMBER: 1994128868
TITLE: Successful **treatment** of chronic bullous **dermatosis** of childhood with colchicine.
AUTHOR: Zeharia A.; Hodak E.; Mukamel M.; Danziger Y.; Mimouni M.
CORPORATE SOURCE: Department of Pediatrics B, Beilinson Medical Campus, Children's Medical Center of Israel, Petah Tiqva 49202, Israel
SOURCE: Journal of the American Academy of Dermatology, (1994) 30/4 (660-661).
ISSN: 0190-9622 CODEN: JAADDB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
007 Pediatrics and Pediatric Surgery
013 Dermatology and Venereology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L22 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:641411 HCAPLUS
DOCUMENT NUMBER: 119:241411
TITLE: Use of mannose phosphates for the treatment of fibrotic disorders

Search completed by David Schreiber 308-4292

White PCT/US02/25028

INVENTOR(S): Ferguson, Mark William James
PATENT ASSIGNEE(S): British Technology Group Ltd., UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9318777	A1	19930930	WO 1993-GB541	19930316
W: AU, CA, JP, KR, NO, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
GB 2265310	A1	19930929	GB 1993-5344	19930316
GB 2265310	B2	19960925		
AU 9337590	A1	19931021	AU 1993-37590	19930316
AU 667887	B2	19960418		
ZA 9301869	A	19940916	ZA 1993-1869	19930316
JP 07504909	T2	19950601	JP 1993-516357	19930316
EP 728006	A1	19960828	EP 1993-906680	19930316
EP 728006	B1	20001011		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
GB 2299025	A1	19960925	GB 1996-7420	19930316
GB 2299025	B2	19961127		
IL 105079	A1	19980615	IL 1993-105079	19930316
AT 196847	E	20001015	AT 1993-906680	19930316
ES 2151903	T3	20010116	ES 1993-906680	19930316
US 5520926	A	19960528	US 1994-290939	19940824
NO 9403451	A	19940916	NO 1994-3451	19940916

PRIORITY APPLN. INFO.: GB 1992-5800 A 19920317
GB 1993-5344 A3 19930316
WO 1993-GB541 A 19930316

AB **Mannose**-6-**phosphate** (I) and **Mannose**-1-**phosphate** (II), or a pharmaceutically acceptable salt or bioprecursor thereof, are used for treatment of mammals having a fibrotic disorder assocd. with accumulation of extracellular matrix and with elevated levels of transforming growth factor-.beta.1 or -.beta.2. I and II accelerate wound healing, and I prevents or mitigates scar formation. Efficacy of I and II in animal studies is presented.

L22 ANSWER 12 OF 20 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92183554 EMBASE
DOCUMENT NUMBER: 1992183554
TITLE: Hydroxychloroquine: A guide to usage.
AUTHOR: Carmichael A.J.
CORPORATE SOURCE: Department of Dermatology, University Hospital of Wales, Heath Park,Cardiff, United Kingdom
SOURCE: Journal of Dermatological Treatment, (1992) 3/2 (103-106).
ISSN: 0954-6634 CODEN: JDTREY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 013 Dermatology and Venereology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hydroxychloroquine is a useful, if infrequently prescribed component of

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the dermatology formulary. Review of the literature concerning the pharmacokinetics and the side-effect profile of the drug, suggest that recommendations of the current data sheet concerning the need for regular ophthalmological monitoring make inappropriate demands on the ophthalmology vice. There is also a strong case for the need for a suspension formulation to enable more precise dosage dependent on ideal body weight.

L22 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:415594 HCAPLUS
DOCUMENT NUMBER: 115:15594
TITLE: Preparation of keratinocyte-targeting agents comprising rhamnose- and galactose-carrier conjugates for cosmetics and pharmaceuticals
INVENTOR(S): Denis, Alain; Kieda, Claudine; Monsigny, Michel; Perrier, Pierre; Redziniak, Gerard
PATENT ASSIGNEE(S): Parfums Christian Dior S. A., Fr.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9011069	A1	19901004	WO 1990-FR176	19900316
W: CA, JP, KR, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
FR 2645741	A1	19901019	FR 1989-3628	19890320
FR 2645741	B1	19950623		
CA 2056357	AA	19900921	CA 1990-2056357	19900316
EP 464077	A1	19920108	EP 1990-904856	19900316
EP 464077	B1	19940202		
R: BE, CH, DE, ES, FR, GB, IT, LI, LU, NL				
JP 04504120	T2	19920723	JP 1990-504959	19900316
JP 2856547	B2	19990210		
ES 2051013	T3	19940601	ES 1990-904856	19900316
US 5286629	A	19940215	US 1991-761809	19911104
PRIORITY APPLN. INFO.:			FR 1989-3628	19890320
			WO 1990-FR176	19900316

AB Keratinocyte-targeting agents comprising a carrier (e.g. submicroscopic particle, liposome, macromol. etc.) coupled to a ligand having glycoside residues that bind to membrane receptors on the keratinocytes are prepd. The ligand particularly has .alpha.-L-rhamnose or .alpha.-D-**galactose**-6-**phosphate** residues. The product may contain a substance of interest in, e.g., dermatol. such as a metab. modulator for skin cells. Cosmetic and pharmaceutical compns. contg. such agents are useful in **epidermis** regeneration, for the **treatment** of psoriasis, and for hair regrowth. A suspension of liposomes encapsulating theophylline and carrying surface residues of rhamnose (provided by asiaticoside) was prepd. as a lotion for treating psoriasis. .alpha.-L-Rhamnose was coupled to dipalmitoylphosphatidylethanolamine and the conjugate was used to prep. liposomes. These liposomes targeted keratinocytes and were endocytosed.

L22 ANSWER 14 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
ACCESSION NUMBER: 1980:131664 BIOSIS

Search completed by David Schreiber 308-4292

DOCUMENT NUMBER: BA69:6660
TITLE: THE EFFECT OF TOPICAL CRUDE COAL TAR **TREATMENT** ON UNSTIMULATED HAIRLESS HAMSTER **SKIN**.
AUTHOR(S): FOREMAN M I; PICTON W; LUKOWIECKI G A; CLARK C
CORPORATE SOURCE: DEP. CHEM. PHARMACOL., SCI. DEV. GROUP, ORGANON LAB. LTD:, NEWHOUSE, SCOTL., UK.
SOURCE: BR J DERMATOL, (1979) 100 (6), 707-716.
CODEN: BJDEAZ. ISSN: 0007-0963.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Topical **treatment** of hairless hamster **skin** with crude coal tar induced epidermal thickening; increased labeling index in the basal cell layer; elevated NADP-dependent **glucose**-6-**phosphate** dehydrogenase activity throughout the epidermis; increased squame count, comedo formation and atrophy of the sebaceous glands. UV light fluorescence microscopy of sections of **treated** **skin** suggests that the hair follicle is an important route for skin penetration by coal tar. [Coal tar has been used empirically in the **treatment** of **skin disease** for nearly 2000 yr and is currently in widespread use for the treatment of psoriasis.]

L22 ANSWER 15 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1981:64668 BIOSIS
DOCUMENT NUMBER: BR20:64668
TITLE: BIOCHEMICAL AND HISTOCHEMICAL STUDY OF **GLUCOSE** CONTENT **GLUCOSE** 6 **PHOSPHATE** DEPHOSPHORYLATION AND HYDROLYTIC ACTIVITY OF ATPASE IN SKIN DURING CONTACT WITH NAPHTHALENE LIQUID.
AUTHOR(S): ABIEV G S; SHAKHMAMEDOVA A I
CORPORATE SOURCE: DIV. HISTOL., N. NARIMANOV AZERB. STATE MED. INST., BAKU, USSR.
SOURCE: Azerb. Med. Zh., (1979 (RECD 1980)) 0 (12), 40-46.
CODEN: AZMZA6. ISSN: 0005-2523.
FILE SEGMENT: BR; OLD
LANGUAGE: Russian

L22 ANSWER 16 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1977:247551 BIOSIS
DOCUMENT NUMBER: BA64:69915
TITLE: SULFATASES LYSOSOMES AND DISEASE.
AUTHOR(S): ROY A B
SOURCE: AUST J EXP BIOL MED SCI, (1976) 54 (2), 111-135.
CODEN: AJEBAK. ISSN: 0004-945X.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable
AB The properties of several purified sulfatases and the deficiency diseases associated with them were discussed. Mammalian sulfatase isolated from ox liver, human urine and liver is an acidic glycoprotein with a high proline content and a MW of .apprx. 100,000 at pH 7, which reversibly self-associates at lower pH values and which is made up of 2 similar subunits of MW .apprx. 50,000. Sulfatase can hydrolyse nitrocatechol sulfate, aryl sulfate and ascorbic acid 2-sulfate. The most powerful known inhibitor of sulfatase A is SO32-, a competitive inhibitor. Sulfatase A also has cerebroside sulfatase activity in the presence of a bile salt and Mn2+ and is capable of hydrolysing other lipids containing **galactosyl** 3-**phosphate** residues: seminolipid, psychosine sulfate and lactosyl sulfate. During hydrolysis of nitrocatechol sulfate sulfatase A is converted into an inactive form which can be reconverted by SO42- and by some other anions. The sulfatase B of ox liver has been

obtained as a homogeneous protein but, unlike sulfatase A, exists in a number of closely related forms (BIx, BiB). It is a glycoprotein with a high proline content and contains high amounts of lysine and arginine. The MW for the 2 fractions was 47,000. Sulfatase B has shown arylsulfatase, N-acetylgalactosamine 4-sulfatase and cerebroside activity. Sulfatase C has been identified as a microsomal arglsulfatase. It also shows steroid sulfatase activity. A number of rare metabolic diseases are associated with sulfatase defects. Metachromatic leucodystrophy, or sulfatide lipidosis, is characterized by degeneration of the myelin associated with an accumulation of cerebroside sulfate due to a deficiency of sulfatase A. Maroteaux-Lamy syndrome (Mucopolysaccharidosis VI) results in the accumulation and excretion of large **amounts** of **mucopolysaccharides**, mainly **dermatan** sulfate, and is due to a deficiency of sulfatase B. Hunter syndrome (Mucopolysaccharidosis II) is characterized by a degradation of dermation and heparan sulfate and deficient of a sulfoiduronate sulfatase activity. SanFilippo A syndrome (Mucopolysaccharidosis III) exhibits an excretion of heparin sulfate and a heparin sulfate N-sulfatase activity is lacking: Morquio's syndrome (Mucopolysaccharidosis IV) is a defect in the degradation of Keraton and chondroitin sulfates and the fibroblast are deficient in a N-acetyl-galactosamine G-sulfatase activity. Multiple sulfatase deficiency is the result of arylsulfatase and steroid inactivity which causes a buildup of cerebroside sulfate, steroid sulfates and polysaccharide sulfates. Placental sulfatase deficiency causes a reduced estrogen excretion during pregnancy which was associated with a placental steroid sulfatase deficiency.

L22 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:69422 HCAPLUS
DOCUMENT NUMBER: 84:69422
TITLE: D-Penicillamine in dermatology. Influence on enzymic activities of human skin in vitro
AUTHOR(S): Raab, W.; Gmeiner, B.
CORPORATE SOURCE: Dep. Med. Chem., Univ. Med. Sch., Vienna, Austria
SOURCE: Arch. Dermatol. Res. (1975), 254(1), 87-93
CODEN: ADREDL
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A dose-dependent activation by D-penicillamine [52-67-5] was obsd. with **glucose**-6-**phosphate** dehydrogenase [9001-40-5] and acid phosphatase [9001-77-8] activities: a dose-dependent inhibition by penicillamine was found with alk. phosphatase [9001-78-9] and glyceraldehyde-3-phosphatedehydrogenase [9001-50-7] activities. Lactate dehydrogenase [9001-60-9] and leucine amino peptidase [9001-61-0] activities remained unchanged in the presence of penicillamine in concns. up to 10 mg/ml. From the data of pharmacokinetic studies in rats it may be concluded that concns. of penicillamine which influence enzymatic activities may easily be reached in vivo in treatment of rheumatoid arthritis and Morbus Wilson. The biochem. actions of penicillamine are briefly discussed with special regard to **therapy** and side effects in **skin disease treatment**.

L22 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1973:451346 HCAPLUS
DOCUMENT NUMBER: 79:51346
TITLE: Carbohydrate metabolism in the involved psoriatic epidermis
AUTHOR(S): Ohkawara, Akira; Halprin, Kenneth M.
CORPORATE SOURCE: Sch. Med., Univ. Miami, Miami, Fla., USA

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SOURCE: Psoriasis, Proc. Int. Symp. (1971), 239-54. Editor(s): Farber, Eugene M. Stanford Univ. Press: Stanford, Calif.. CODEN: 26UYA8
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with conclusions. Carbohydrate metab. is generally increased in the psoriatic epidermis. Among pathways of carbohydrate metab. the hexose monophosphate shunt is highly accentuated. Increased **glucose** 6-**phosphate** utilization through the hexose monophosphate shunt provides NADPH for the reductive synthetic reactions and provides ribose for the nucleic acid and nucleotide formation in the rapidly proliferating psoriatic cells. The overall metabolic pattern is not specific to psoriasis, and it can occur in other situations with increased epidermal turnover rate such as **epidermolytic** hyperkeratosis and **exfoliative dermatitis** of any cause. Increased glycogen content in the psoriatic epidermis could be due to (1) a great increase in a rate of synthesis (high total glycogen synthetase activity) as compared to the relatively moderate increase of its degradn. (phosphorylase) or (2) a low level of adenyl cyclase and a resulting low cyclic AMP concn. 32 refs.

L22 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1970:77339 HCAPLUS
DOCUMENT NUMBER: 72:77339
TITLE: Glyceraldehydephosphate dehydrogenase and **glucose**-6-**phosphate** dehydrogenase activities in psoriasis and neurodermatitis and the effect of dithranol
AUTHOR(S): Hammar, Hans
CORPORATE SOURCE: Dermatol. Histol. Dep., Univ. Uppsala, Uppsala, Swed.
SOURCE: J. Invest. Dermatol. (1970), 54(2), 121-5 CODEN: JIDEAE
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The subcorneal and basal parts of the human germinal epithelium weremicrodissected from freeze-dried sections originating within or just outside guttate psoriatic and neurodermite lesions. Glyceraldehydephosphate dehydrogenase (GAPDH) (EC 1.2.1.12) and **glucose**-6-**phosphate** dehydrogenase (G6PDH) (EC 1.1.1.49) were measured by Lowry's microtechniques and displayed a similar pattern, with a significant increase in the uninvolved part of the border region of the psoriatic lesion and a greater increase within the lesion. In the neurodermite lesion an increase was obtained only within the lesion and the 2 activities correlated but were lower than those encountered in psoriasis. After treatment with dithranol (1,8,9-trihydroxyanthracene) (0.1 dithranol, 2 salicylic acid, 12 ZnO, 12 starch, and white petroleum to 100 g), the 2 enzymic activities in the psoriatic epidermis were depressed in the border region of the blanched nonscaling lesion and within the lesion. GAPDH activity decreased only in the basal epidermis. G6PDH showed decreased activity within the treated lesion in boththe subcorneal and basal parts of the **epidermis**, and after **treatment** correlation between activities of the 2 enzymes could no longer bedetected.

L22 ANSWER 20 OF 20 MEDLINE
ACCESSION NUMBER: 67213814 MEDLINE
DOCUMENT NUMBER: 67213814 PubMed ID: 4226875
TITLE: [Activity of serum phosphohexose isomerase in some skin

diseases].
Aktivnost' syvorotochnoi fosfogeksozoizomerazy pri nekotorykh kozhnykh zabolevaniiakh.

AUTHOR: Turkevich A N
SOURCE: VRACHEBNOE DELO, (1966 Jan) 1 86-8.
Journal code: 0413607. ISSN: 0049-6804.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196710
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19980206
Entered Medline: 19671014